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TITLE: Computer Assisted Cancer Device - 3D Imaging

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14. ABSTRACT The technical objective of the Computer Assisted Cancer Device project is to develop a platform technology that will allow for a significant improvement in the accuracy of interpreting mammograms through the use of Second Generation Computer Assisted Detection (2 nd Generation CAD) that is designed for using not only the current year's screening mammograms (as is common in first generation commercial CAD) but also any additional clinically relevant information (e.g. prior mammograms, other sensors like 3D ultrasound/MRI/IR, participant history, etc.). This 2 nd Generation CAD platform will be used to provide "procedure based" CAD advice to the doctors.					
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**Computer Assisted Cancer Device—3D Imaging
Annual Technical Report
USAMRAA Award Number: W81XWH-05-2-0039**

Report Period: March 1, 2005 through February 28, 2006

**Principle Investigator: Albert V. Porambo, LTC, MC
Collaborators: Steve Worrell and Kevin Woods
Michael Liebman**

1. INTRODUCTION:

The technical objective of the Computer Assisted Cancer Device project is to develop a platform technology that will allow for a significant improvement in the accuracy of interpreting mammograms through the use of Second Generation Computer Assisted Detection (2nd Generation CAD) that is designed for using not only the current year's screening mammograms (as is common in first generation commercial CAD) but also any additional clinically relevant information (e.g. prior mammograms, other sensors like 3D ultrasound/MRI/IR, participant history, etc.). This 2nd Generation CAD platform will be used to provide "procedure based" CAD advice to the doctors. This will be accomplished by adding a 3-D breast ultrasound examination to the pre-biopsy evaluation of all study participants as a way of adding additional input to the development of the CAD algorithm. Since breast ultrasound is a safe, non-invasive modality, it may be able to significantly improve the positive predictive value of breast biopsies if an algorithm can be successfully created.

It is well documented that breast cancer is frequently missed on mammograms leading to delayed detection and potentially less successful treatment. Our studies show that approximately 32% of cancers can be detected earlier in mammograms. While current CAD technology is designed to capture as many of these cancers as possible, it is not able to offer specific information in order to assist the radiologist in determining the best course of action once a suspicious region is identified. (2) The use of additional information will allow the 2nd Generation CAD system to provide the decision support information needed for making the best decision. Approximately 4.6 billion dollars was spent conducting biopsies in 2002 and only 10-30% of these biopsies resulted in the diagnosis of breast cancer. The use of all of the available sensor and participant history data will allow the elimination of a significant number of these unnecessary biopsies and the concomitant benefit of reduced trauma and anxiety for participants who currently endure them. Breast ultrasound is a safe, non-invasive way of obtaining additional information about the participant's breasts that will be added to the other imaging modalities already in use clinically. The data will be able to be digitized and analyzed, as the 1st generation CAD does for mammograms.

We propose to fundamentally improve the detection, diagnosis and treatment of breast cancer by developing a platform technology that will allow for a significant improvement in the accuracy of interpreting mammograms through the use of Second Generation Computer Assisted Detection (2nd Generation CAD) that is designed for using not only the current year's screening mammograms (as is common in first generation commercial CAD) but also any additional clinically relevant information (e.g. prior exams, other sensors like 3D ultrasound/Magnetic Resonance Imaging, participant history information, etc.). Specifically in this study, 3-D ultrasound will be added to the modalities already used in the clinical care of enrolled participants. Using the additional sources of information will help move CAD technology from being a detection aid to becoming a diagnostic aid.

The overall project is expected to require 2 years with the following phases:

1. Initial data collection, (please note: the only data collected will be the results of the ultrasound images identified by CBCP number) system modification and preliminary testing (12 months).
2. System refinement and additional testing (6 months).
3. Clinical testing (6 months).

2. BODY:

1. A award of 900,000 dollars was awarded from 3/1/05 – 2/28/06.
2. A modification was issued extending the period of performance from 3/1/05 to 10/31/06 (Research ending 30 September 06) and increasing the funding by \$1,006,484 from \$900,000 to \$1,906,484.
3. AIBS (The American Institute of Biological Sciences' SPARS Division - an independent, impartial peer review and scientific support organization) reviewed the proposal identifying strengths and weaknesses in July of 2004.
4. A letter dated 10/14/04 from Patricia A. Evans, Contracting/Grant Officer informs Albert V. Porambo, LTC, MC that responses to the critique are satisfactory and the work is recommended for funding.
5. A protocol was drafted and submitted to the WRAMC Department of Clinical Investigation on 10/4/04.
6. The protocol was approved by the Clinical Investigation Committee on 11/16/04.
7. The protocol was approved by the Human Use Committee 12/14/04.
8. The protocol was approved by CIRO on 4/6/05.

9. The protocol was approved for a total of 1000 subjects – 750 enrolled at WRAMC and 250 enrolled at the Joyce Murtha Breast Center in Windber, PA.
10. Funding through CRADA approved by CIRO 3/31/05. The CRADA is with Henry M. Jackson Foundation and the sponsor is the Department of Army, US Army Medical Research Acquisition Activity.
11. The GE 4-D logic ultrasound unit was purchased for WRAMC in April 2005.
12. The GE 4-D logic ultrasound unit was purchased for the Joyce Murtha Breast Care Center in July 2005. The unit was calibrated and subsequent evaluation by Windber Medical Center radiologists indicated that there were apparent problems associated with its resolution and this negatively impacted its potential use.
13. Despite advertisements placed as early as January 2005, an ultrasound tech was not hired until June 13 2005 to begin work June 27, 2005. Originally, training with GE (manufacturer of the 3D Ultrasound machine) was arranged for July 5, 2005. Training for the US tech was scheduled for August 18th, 2005. Kevin Woods, iCAD Inc., Kristin Laconte and Michael Washburn, GE Healthcare Ultrasound Unit, attended the training session to define the imaging protocol, discuss data format and transfer options. The specification was for each 2D view of a candidate lesion to be captured with different settings on the 3D US machine, and for each 3D view, two volumes would be captured with different machine settings. Although trained on the newly purchased ultrasound machine, work could not begin as the protocol was still in the approval process. The ultrasound technician was terminated from employment in August 2005 for repeated absenteeism.
14. Once approval from CIRO was obtained, the protocol was submitted to MRMC for secondary review. Revisions were requested on May 10, 2005, June 27, 2005, August 2, 2005. An addendum dated September 2, 2005 was submitted to the WRAMC DCI to incorporate revisions made by MRMC/TATRC HSRRB into the protocol WU # 05-47007. The addendum was approved on November 17, 2005.
15. The first Annual Progress Report was approved 11/22/05. Work had not yet begun on the project.
16. In December of 2005, iCAD was informed that the mammography portion of the data collection protocol had been removed from the project scope. As a consequence, it was decided only 3D ultrasound data would be collected for the purpose of developing CAD algorithms.
17. Another search began for a second ultrasound tech in January 2006.
18. In January of 2006, Kevin Woods and Steve Worrell, iCAD Inc., were informed by Walter Reed that the WRAMC would require them to undergo Human

Subjects Training before the IRB would approved the protocol. Both Kevin Woods and Steve Worrell completed their Human Subject Training by January 6, 2006. The training certificates were forwarded to the WRAMC.

3. KEY RESEARCH ACCOMPLISHMENTS

19. Since the 3D Ultrasound Units at Walter Reed and Windber were GE machines, GE expressed interest in jointly developing CAD. The technical staff within the GE Ultrasound Unit helped to develop the imaging protocol that would be used for data collection. The business arrangement was put on hold until data collection could begin and a proof of concept CAD algorithm could be developed.
20. Data collection efforts under this project have been challenging and additional time was required to install the equipment, approve data collection protocols and hire appropriate personnel. While Ultrasound and other data from Walter Reed Army Medical Center is just beginning to be collected and Windber Research Institute is awaiting protocol approval to perform the planned research, iCAD was able to initiate the research effort using 3D tomosynthesis images of the breast. iCAD has identified several sources of 3D tomosynthesis data, and has begun adapting its image analysis techniques to operate on 3D data. iCAD is able to acquire tomosynthesis data that is not currently widely available to other institutions due to our collaborative relationships with major manufacturers of tomosynthesis equipment.
21. iCAD believes that tomosynthesis, a 3D breast imaging technique using x-ray radiation, is very promising and anticipate that it will play an important role in achieving the research objectives of this project. The purported advantages of tomosynthesis relative to conventional mammography include; improved lesion visibility, improved lesion detectability and reduction of negative biopsies. iCAD believes that the full potential of tomosynthesis will require sophisticated 3D CAD algorithms and that iCAD's existing mammography image analysis product (Second Look) provides a powerful platform for extension to this application.

4. REPORTABLE OUTCOMES

There are no reportable outcomes to date.

5. CONCLUSIONS

22. The Joyce Murtha Breast Care Center received and had installed the GE 4-D logic 9 ultrasound Unit as part of the ICAD – CBCP – WRI project.

23. The unit was calibrated and subsequent evaluation by WMC staff radiologists indicated that there were apparent problems associated with its resolution and negatively impacted its potential use.

24. These problems have been recently rectified by GE technicians and the radiology group has acknowledged the status of the unit as being operational.

25. Interviewing for the ultrasound technician is underway.

26. Simultaneously, the protocol for its use in the ICAD study is being finalized for submission to the IRB for review in September following its lengthy review and re-review cycle involving WRAMC and Ft. Detrick Human Use Committee. This is standard protocol for the Windber IRB to wait for the WRAMC-Ft Detrick acceptance before preparation and submission to its IRB

6. REFERENCES

N/A

7. APPENDICIES

ATTACHMENT 1 Project Quarterly Expenditures Breakout

**ATTACHMENT 1: Project Computer Assisted Cancer Device—3D Imaging
Quarterly Expenses breakout**

Contract Expenditures Year 1

Cost Elements	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter	Cumulative
Personnel	\$0.00	\$8,697.18	\$0.00	\$0.00	\$8,697.18
Fringe Benefits	\$0.00	\$2,478.70	\$0.00	\$0.00	\$2,478.70
Supplies	\$0.00	\$137,350.00	\$64.60	\$3,499.58	\$140,914.18
Equipment	\$233,284.81	\$212,734.61	\$7,345.39	\$0.00	\$453,364.81
Travel	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00
Other Direct Costs	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00
Sub Awards	\$0.00	\$6,116.72	\$14,198.21	\$0.00	\$20,314.93
Subtotal	\$233,284.81	\$367,377.21	\$21,608.20	\$3,499.58	\$625,769.80
Indirect Costs		\$6,706.68	\$11.21	\$609.28	\$7,327.17
Fee		\$0.00	\$0.00	\$0.00	\$0.00
Total	\$233,284.81	\$374,083.89	\$21,619.41	\$4,108.86	\$633,096.97